View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Elsevier - Publisher Connector

Many Patients 80 Years and Older with Advanced Non-small Cell Lung Cancer (NSCLC) Can Tolerate Chemotherapy

Ozden Altundag, MD, David J. Stewart, MD,* Frank V. Fossella, MD,* Gregory D. Ayers, MS,† Wei Wei, MS,† Xian Zhou, PhD,† and Ralph G. Zinner, MD**

Abstract: People 80 years of age and older constitute 17.8% of all lung cancer patients in the United States. Because the life expectancies of 80-year-old men and women are 87.3 years and 89.0 years, respectively, non-small cell lung cancer shortens lives in addition to causing morbidity. In this retrospective study, all patients with chemotherapy-naive advanced non-small cell lung cancer 80 years of age and older treated at the M. D. Anderson Cancer Center with one or more follow-ups were identified from the database for the years 1997 to 2004. A cohort of patients younger than 80 years old was matched based on treatment year, race, histology, and gender in a 2:1 ratio. Of 13,690 thoracic oncology patients, 496 (3.6%) were 80 years of age and older, of whom 46 met the criteria. In older and younger patients, respectively, platinum doublets were given in 43% versus 79% ($p < 0.0001$), the response rate was 41% versus 47%, the median progression-free survival was 5.55 versus 3.91 months ($p = 0.216$), and the median overall survival was 10.7 versus 9.8 months ($p = 0.43$). Hematologic and nonhematologic toxicities were similar. Our data indicate that selected patients 80 years of age and older may tolerate and benefit from chemotherapy, and prospective evaluation of these patients is indicated.

Key Words: Non-small cell lung cancer, Advanced, Elderly, 80 years old, Chemotherapy.

(*J Thorac Oncol.* 2007;2: 141–146)

Lung cancer is the most common cancer in the world and the leading cause of cancer-related deaths in Western countries.[1] Non-small cell lung cancer (NSCLC) represents 80% to 85% of all lung cancers. Approximately 40% to 50% of these patients present with incurable metastatic (stage IV) disease.[2] Most of what we know about the treatment of advanced NSCLC has been learned from studies of patients largely younger than 70 years old.

Platinum-based chemotherapy has been shown to both increase overall survival and improve the quality of life in patients with an adequate performance status (PS).[3,4] A recent study showed that bevacizumab improves survival when added to paclitaxel/carboplatin in patients with nonsquamous NSCLC.[5] Additionally, second-line agents such as docetaxel and pemetrexed improve survival and quality of life,[6,7] and erlotinib improves survival when given as a second- or third-line agent.[8]

It is uncertain how well older patients respond to these chemotherapies, and there is concern about the safety of treating them. It is important to acquire a better understanding of the impact of chemotherapy on the elderly because >50% of cases of advanced NSCLC are diagnosed in patients 70 years of age and older (median age is 70 years old).[9] Although the percentage of patients 70 years and older in phase III trials has been 12% to 27%, a number of retrospective subset analyses of phase III trials have shown a survival benefit in patients 70 years of age and older.[10] A phase III trial by Lilenbaum et al.[11] studying paclitaxel/carboplatin versus paclitaxel was stratified for patients older than 70 years of age and showed a statistically improved response rate and time to progression, although it did not show improved overall survival ($p = 0.289$). Based on these data, it is believed to be appropriate to treat selected patients older than 70 years of age with platinum doublets. A phase II study showed that vinorelbine plus gemcitabine in chemotherapy-naive NSCLC patients 80 years of age and older (12 of 20 patients with advanced disease) was tolerated and showed activity.[12]

Although there are limited data on the effectiveness and safety of chemotherapy for patients 70 years of age and older, there are almost no data for patients 80 years of age and older, even though they constitute 17.8% of all lung cancer patients (80–84 years, 10.98%; 85+ years, 6.85%) in the United States, according to the Surveillance Epidemiology and End Results program reported in 2004 (data from years 1973 to 2002 varying) (According to a conversation with Milt Eisner, Health Statistician at Cancer Statistics Branch, Surveillance Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, MD on

Departments of *Thoracic/Head and Neck Medical Oncology and †Statistics and Applied Mathematics, The University of Texas M. D. Anderson Cancer Center, Houston, TX.

Address for correspondence: Ralph G. Zinner, MD, Department of Thoracic/Head and Neck Medical Oncology, Unit 432, The University of Texas M. D. Anderson Cancer Center, Houston, TX 77030. E-mail: rzinner@mdanderson.org

Copyright © 2007 by the International Association for the Study of Lung Cancer

ISSN: 1556-0864/07/0202-0141

June 16, 2005) and are likely to continue to grow as a fraction of the NSCLC population.

Moreover, from actuarial tables of the population at large, the life expectancies of 80-year-old men and women are 87.3 and 89.0 years, respectively.[13] In addition only a minority of these 80 years of age and older and 85 years of age and older have dementia.[14,15] Advanced NSCLC not only causes morbidity but may also rob them of many years meaningful of life. Therefore, it is important to learn whether there is a role for chemotherapy in these patients. We present data from a retrospective review of the outcome of all NSCLC patients 80 years and older who were treated at The University of Texas M. D. Anderson Cancer Center (MDACC) between 1997 and 2004 compared with matched control patients younger than 80 years old.

PATIENTS AND METHODS

The MDACC Surveillance Committee (institutional review board) approved our retrospective review of the patients' medical records for this study. A list of all thoracic oncology patients registered at MDACC between 1997 and 2004 was obtained. The registry includes age, gender, race, histology, and date of registration. To study these patients, we identified both a group of patients 80 years of age and older and a group of matched controls made up of patients younger than 80 years old. We first identified the patients 80 years of age and older seen at MDACC between the years of 1997 and 2004, the years covered in the registry. We then identified the subset of these patients who had advanced (stages IV and III with malignant effusions) chemotherapy-naive NSCLC treated at MDACC at least once with systemic therapy with at least one follow-up. We studied a uniform population so our results would be more interpretable. Once these patients were identified, we then formed a control of patients younger than 80 years old matched by histology, race, gender, and same year of first chemotherapy with the 80 years of age and older patients. To do this, the database was placed on an Excel spreadsheet. Once the patient list was sorted by histology, race, and admission date, the database was searched patient by patient until two matched controls of patients younger than 80 years old were identified. We then did a chart review to collect data on PS, weight loss, first-line chemotherapy regimen, toxicity, dose delay, dose reduction, date of first chemotherapy, and whether second-line chemotherapy was given. We also evaluated whether patients received a standard dose of chemotherapy from clinical notes. Clinical response to first-line chemotherapy was defined as any decrease in tumor volume based on clinical and radiographic assessments and included both partial remissions and minor responses (tumor shrinkage $<$ partial remission).

As a separate question, we looked at whether patients 80 years of age and older registered at MNACC had a different likelihood of being treated here compared with younger patients. We calculated the percentage of patients with chemotherapy-naive advanced NSCLC from each age group (younger than 80 years of age versus 80 years of age and older) who had received at least one cycle of chemotherapy and had come to MDACC for at least one follow-up visit. Because the number of patients younger than 80 years old in the database was large, we looked at a subset as follows. We identified another group of patients different from the younger than 80 years old matched controls mentioned above. To do this, we again looked at the 13,194 patients younger than 80 years old in the database. From this, we randomly selected a subset of 1100 patients from this group by sorting by registration date and then selecting every 12th patient from the list. From these 1100 patients, we identified a subset of patients with advanced NSCLC who were chemotherapy-naive on presentation and calculated the proportion of these patients who received at least one cycle of chemotherapy and one follow-up visit at MDACC.

Statistical Analysis

The associations between categorical variables were assessed via cross tabulation, the χ^2 test, or the Fisher exact test as appropriate. Patient characteristics were analyzed for their associations with time-to-event by using the stratified Cox proportional hazards progression model, which was used because of the paired nature of the data set. Overall survival was defined as the time from the date of the first chemotherapy to the time of death from any cause. Progression-free survival was defined as the date of chemotherapy to the date of progression or death from any cause. Patients alive and progression free at the date of last follow-up were censored. Estimates of survival curves were calculated according to the Kaplan–Meier product-limit method. The distribution of survival times between patients with different characteristics was compared by means of the log-rank test. Variables with p values <0.10 from the univariate Cox proportional hazards model were included in a multivariate model. All computations were carried out on a D PC using the Windows NT operating system in SAS (SAS Institute, Inc., Cary, NC) and S-plus 2000 (Cambridge, MA) (SAS Institute Inc., SAS/STAT Users Guide, Version 8).

RESULTS

The likelihood of patients 80 years of age and older being treated compared with the control cohort of patients younger than 80 years old is presented here. There were 13,690 lung cancer patients registered in the MDACC database between 1997 and 2004. Among them, 496 patients (3.6%) were 80 years of age and older at the time of registration. Of these 496 patients, 140 (28%) had advanced chemotherapy-naive NSCLC, and of these, 46 of 140 (33%) were treated and had at least one follow-up at MDACC. From a cohort of 1100 randomly selected patients younger than 80 years old, 315 (29%) had advanced chemotherapy-naive NSCLC and 109 of 315 (35%) of patients in the control group (younger than 80 years old) were treated at MDACC and had at least one follow-up.

The data assessing outcome by comparing the 80 years of age and older cohort with the matched controls of patients younger than 80 years old are presented here. In the control (younger patients), 87 of 92 (95%) were perfect matches with the study group (older patients) for the characteristics we controlled for (Table 1). Of the five patients who did not fully match, four had received chemotherapy at least 1 year later

 Copyright © 2007 by the International Association for the Study of Lung Cancer

TABLE 1. Patient Clinical Characteristics Grouped by Age

	No. (%) of Patients			
	Any Systemic Therapy		Platinum Doublet	
	Age <80 (n = 92)	Age ≥80 (n = 46)	Age <80 (n = 73)	Age >80 (n = 20)
Gender				
Female	46 (50)	23 (50)	37 (50.6)	10 (50)
p	1.00		1.00	
Race				
African American	4 (4.3)	2 (4.3)	3 (4)	0 (0)
Hispanic	3 (3.2)	2 (4.3)	2 (2.7)	0 (0)
White	85 (92.3)	42 (91.3)	68 (93)	20 (100)
p	0.95		1.00	
Pathology				
Adenocarcinoma	38 (41.3)	19 (41.3)	32 (43.8)	9 (45)
BAC	12 (13)	6 (13)	8 (10.9)	3 (15)
Squamous	14 (15.2)	7 (15.2)	13 (17.8)	2 (10)
LCUD	28 (30.4)	14 (30.4)	20 (27.3)	6 (30)
p	1.00		0.86	

BAC, bronchioloalveolar carcinoma; LCUD, large cell undifferentiated.

TABLE 2. Patient Performance Status and Weight Loss Grouped by Age

	No. (%) of Patients			
	Any Systemic Therapy		Platinum Doublet	
	Age <80 (n = 92)	Age ≥80 (n = 46)	Age <80 (n = 73)	Age ≥80 (n = 20)
PS				
0 or 1	71 (77.2)	27 (58.7)	60 (82.2)	17 (85)
2 or 3	16 (17.4)	16 (34.8)	9 (12.3)	2 (10)
NA	5 (5.4)	3 (6.5)	4 (5.5)	1 (5)
p	0.02		1.00	
Weight loss				
<5%	64 (69.6)	31 (67.4)	54 (74)	16 (80)
5–10%	12 (13)	9 (19.6)	7 (9.6)	4 (20)
≥10%	16 (17.4)	2 (4.3)	12 (16.4)	0 (0)
NA	0 (0)	4 (8.7)	0 (0)	0 (0)
p	0.09		0.07	
Smoking history				
Never smoked	15 (16.7)	11 (24.4)		
Ever smoked	75 (83.3)	34 (75.6)		
p	0.35			

PS, performance status; NA, not available.

than the matched patients in the older group (minimum, 13.4 months; maximum, 22.4 months). The fifth patient was a non-Hispanic white who was matched with a Hispanic patient.

The older and younger groups were then further characterized. The median ages of the older and younger groups were 82 years (range, 80–88) and 65 years (range, 28–79), respectively. PS was 0 or 1 in 62.8% and 81.6% of patients in the older and younger groups, respectively. ($p = 0.02$). Weight loss in the previous 6 months was comparable for both groups ($p = 0.09$) (Table 2).

Older patients received platinum doublets less frequently than younger patients (43% versus 79%, $p < 0.0001$). Sixteen (35%), seven (15%), and three (7%) patients in the older group received a single-agent chemotherapy (vinorelbine, gemcitabine, or docetaxel), gefitinib only, or a nonplatinum doublet treatment as a first-line chemotherapy, respectively. In contrast, in younger group, six (7%), eight (9%), and five (5%) patients received single-agent chemotherapy (gemcitabine, mitomycin, vinorelbine, paclitaxel, or docetaxel), gefitinib only, or a nonplatinum doublet as a first-line chemotherapy, respectively. Standard doses of chemotherapy were given to almost all patients in the older and younger groups (93.4% versus 94.5%) ($p = 1.00$). The median number of cycles of first-line chemotherapy for older and younger patients was four (range, 1–27) and three (range, 1–14) cycles, respectively. Dose reduction was not significantly different between the older and younger groups (21.7% versus 14.1%, $p = 0.26$). Chemotherapy was delayed due to toxicity at least once in nine (19.6%) and 18 (19.5%) patients in the older and younger groups, respectively ($p = 1.00$). The rate of use of at least one granulocyte colony-stimulating factor treatment was 8.7% in the older and 6.5% in the younger group ($p = 0.73$). A clinical response was observed in 19 (41%) patients in the older group and 43 (47%) patients in the younger group. Although there were no radiographic reports for one patient in each group, clinical notes were taken into consideration for response evaluation. The rate of second-line chemotherapy was also similar for both older and younger patients (41.3% versus 44.6%, $p = 0.72$) (Table 3).

Hematologic and nonhematologic toxicities were not significantly different between older and younger patients (Table 4). Grade 3/4 hematologic toxicity was documented in six (13%) and 16 (17.4%) patients in the older and younger groups, respectively ($p = 0.63$). Grade 3/4 nonhematologic toxicity was documented in seven (15.2%) and 23 (25%) patients in the older and younger groups, respectively ($p = 0.27$). These observations held up when controlling for platinum-based chemotherapy (hematologic toxicity, $p = 0.29$; nonhematologic toxicity, $p = 0.38$) (Table 4).

Fourteen (30%) patients in the older group and 25 (27%) patients in the younger group completed six cycles of first-line chemotherapy. Nine (20%) patients in the older group and 14 (15%) patients in the younger group elected to stop before six cycles because of toxicity ($p = 0.68$). In the older group, these toxicities were neuropathy (two patients, one with grade 2 and the other with grade 3), fatigue (four patients with grade 3), and neutropenia with or without infection (three patients with grade 4). In the younger group, the reasons for stopping first-line chemotherapy early because of toxicity were neutropenic fever (three patients), grade 4 neutropenia (two patients), nausea and vomiting (one with grade 2 and the other with grade 3), peripheral neurotoxicity (three patients with grade 3), and other toxicities (four patients). Two (4.3%) older patients died after the administra-

Copyright © 2007 by the International Association for the Study of Lung Cancer

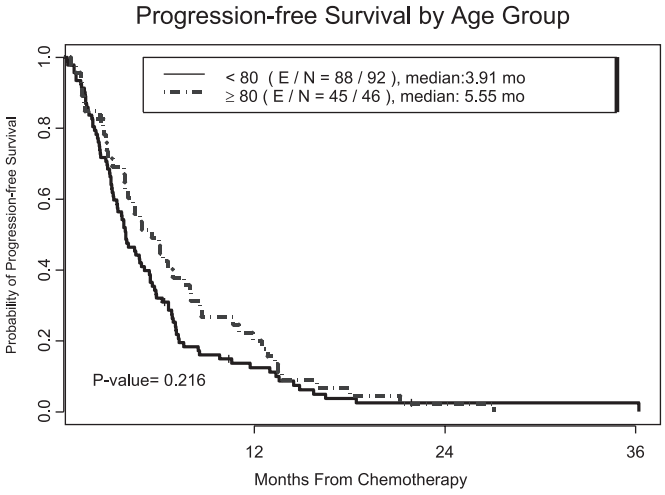
TABLE 3. Patient Treatment Characteristics Grouped by Age

	No. (%) of Patients			
	Any Systemic Therapy		Platinum Doublet	
	Age <80 (n = 92)	Age ≥80 (n = 46)	Age <80 (n = 73)	Age ≥80 (n = 20)
Dose reduction				
Yes	13 (14.1)	10 (21.7)	12 (16)	5 (25)
p	0.26		0.51	
Chemotherapy cycle delay				
Yes	18 (19.5)	9 (19.6)	17 (23)	4 (20)
p	1.00		1.00	
Standard dose				
Yes	87 (94.5)	43 (93.4)	70 (96)	18 (90)
p	1.00		0.29	
G-CSF use				
Yes	6 (6.5)	4 (8.7)	5 (7)	2 (10)
p	0.73		0.64	
Second-line chemotherapy				
Yes	41 (44.6)	19 (41.3)	35 (48)	12 (60)
p	0.72		0.45	

G-CSF, granulocyte colony-stimulating factor.

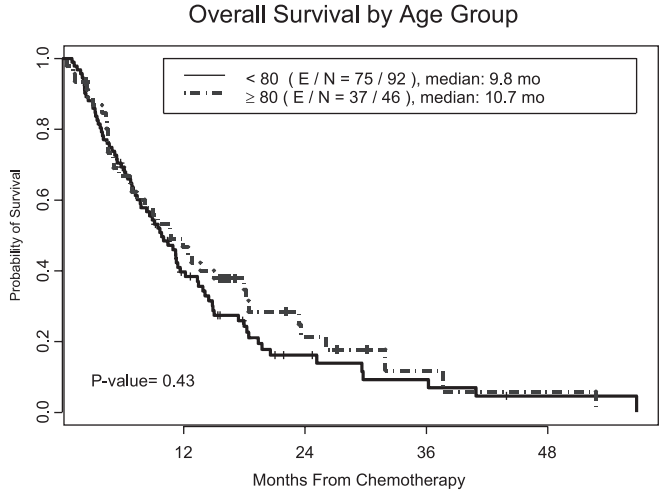
TABLE 4. Patient Toxicity Profiles Grouped by Age

	No. (%) of Patients			
	Any Systemic Therapy		Platinum Doublet	
	Age <80 (n = 92)	Age ≥80 (n = 46)	Age <80 (n = 73)	Age ≥80 (n = 20)
Grade 3/4 hematologic toxicity				
Yes	16 (17.4)	6 (13)	12 (16.4)	1 (5)
p	0.63		0.29	
Grade 3/4 nonhematologic toxicity				
Yes	23 (25)	7 (15.2)	20 (27.4)	3 (15)
p	0.27		0.38	



E, Events; N, Total patient number

FIGURE 1. Kaplan–Meier estimates of progression-free survival grouped by age. E, events; N, total number of patients.



E, Events; N, Total patient number

FIGURE 2. Kaplan–Meier estimates of overall survival grouped by age. E, events; N, total number of patients.

tion of the first cycle of chemotherapy; one died of neutropenic sepsis and the other died of unknown causes. Two (2.1%) younger patients died after the first chemotherapy cycle. One died of ischemic bowel perforation, and a second younger patient died of an unknown cause.

Events (tumor progression or death from any cause) were noted in 45 of 46 (98%) older patients and 88 of 92 (96%) younger patients. The median progression-free survival for older and younger patients were 5.55 (95% confidence interval [CI]: 3.88–8.02) and 3.91 (95% CI: 3.35–5.45) months (p = 0.216), respectively (Figure 1). In the univariate analysis, older patients tended to have better progression-free survival than younger patients (hazard ratio = 0.63 [95% CI: 0.39–1.02]; p = 0.06).

As of this writing, 37 of 46 (80%) and 75 of 92 (82%) deaths have occurred in the older and younger patient groups, respectively. The median overall survival was 10.7 (95% CI: 6.87–18.2) months for the older patients and 9.8 (95% CI: 7.72–13.4) months for the younger patients (Figure 2) (p = 0.43). Overall survivals of the older and younger patients according to the PS and whether they received platinum-based chemotherapy are summarized in Table 5. Survival analyses by the multivariate Cox proportional hazard model were done controlling for PS, weight loss, and smoking status. Weight loss of >5% predicted worse survival in patients ≥80 (HR = 3.11, p = 0.02) but did not reach significance in patients younger than 80 years old (HR = 1.35, p = 0.27). Poor PS did not reach statistical significance for worse survival in patients 80 years and older (HR = 1.78, p = 0.18), but did in patients younger than 80 years old (HR = 2.13, p = 0.01). Ever smoking did not significantly affect survival in patients 80 years and older (HR = 0.720,

Copyright © 2007 by the International Association for the Study of Lung Cancer

TABLE 5. Overall Survival by Factors

Patient Population	Variable	Level	No.	Median (mo)	Rate at 1 yr (%)	*p*
All patients	Overall		138	10.4	42	0.43
	Age	<80	92	9.8	40	
		≥80	46	10.7	47	
PS 0/1	Age	<80	71	11.3	45	0.414
		≥80	27	15.0	58	
PS 2/3	Age	<80	16	4.8	22	0.577
		≥80	16	8.9	25	
PS 0/1 with no platinum	Age	<80	11	9.5	36	0.672
		≥80	10	13.9	60	
PS 0/1 with platinum	Age	<80	60	11.3	47	0.391
		≥80	17	18.5	56	
PS 2/3 with no platinum	Age	<80	7	3.2	14	0.033
		≥80	14	9.5	29	
PS 2/3 with platinum	Age	<80	9	10.9	27	0.196
		≥80	2	7.0	NA	

PS, performance status; NA, not applicable.

$p = 0.50$) or in patients younger than 80 years old (HR = 1.55, $p = 0.24$).

DISCUSSION

We report outcomes of a substantial number of patients with advanced stage NSCLC 80 years of age and older who were treated with chemotherapy. Our results showed that selected patients with advanced NSCLC 80 years and older can tolerate and respond to standard chemotherapy. We also observed that there were similar outcomes in older and younger patients in most of the subsets examined. Moreover, this similarity between the older and younger patients was observed whether patients received platinum-based combination chemotherapy or other chemotherapy. In the case of overall survival, a multivariate analysis controlling for PS, weight loss, and smoking status demonstrated no statistically significant difference. The hematologic and nonhematologic toxicities, number of cycles given, and rate of second-line chemotherapy were similar between the older and younger groups.

First- and second-line chemotherapy have been established as offering survival and quality-of-life benefits to younger patients with advanced NSCLC with an adequate PS.[3,6,7] Because patients 80 years of age and older constitute 17.8% of all lung cancer patients and the median survival of healthy octogenarians is approaching a decade, it is important to consider whether these patients can benefit from chemotherapy. However, there are almost no published data to guide us because very few patients 80 years of age and older are included in phase III trials. Because elderly patients are often believed to be unable to tolerate chemotherapy, they are generally excluded from clinical trials and are typically not considered appropriate for aggressive platinum-based chemotherapy in clinical practice,[16] as revealed in a recent analysis of clinical data from the Southwest Oncology Group.[17] However, an abstract presented in 2005 at the American Society of Clinical Oncology by Hesketh et al.[18] reported outcomes from two first-line advanced NSCLC trials for patients 70 years of age and older: the Southwest Oncology Group (S0027) (sequential vinorelbine and docetaxel) and an investigator-initiated multicenter trial (LUN 6) (single agent docetaxel). Between these trials, the 47 patients (21.5%) who were 80 years of age and older had similar disease control, although the patients with a PS of 0/1 had shorter survival than the younger patients but the very elderly patients with a PS of 2 had a similar overall survival. They noted that the regimens were well tolerated by the patients 80 years of age and older and concluded that selected patients in this age group may benefit from single-agent chemotherapy. In addition, there are recent reports indicating a survival benefit in patients older than 70 years old.[10,19] These data encourage us to investigate whether patients 80 years of age and older might benefit from standard chemotherapy doublets. However, there are substantial concerns about treating older patients. Elderly patients often present with medical and physiologic characteristics[20,21] that make the selection of their optimal treatment more challenging. Moreover, aging causes physiologic changes in functional status, organ function, and drug pharmacokinetics. Furthermore, concomitant diseases, which may significantly affect functional status, general health, and tumor symptoms, are frequently present in this patient population.[22] These comorbidities may also result in a higher prevalence of polypharmacy and related risks.[23] Given these health concerns, it is important to carefully assess the potential benefit.

Our results are encouraging. However, they are only preliminary. This was a retrospective study, so there may be selection bias. Thus, patients 80 years of age and older may have a lesser or greater tendency to be treated, resulting in a population of patients who are in a different condition than the younger patients. However, the national Surveillance Epidemiology and End Results program database has given the percentage of lung cancer patients 80 years of age and older as 17.8%, but our data registry showed that these patients constituted only 3.6% of the MDACC lung cancer population. This difference suggests that MDACC's elderly population may be highly selected and not representative of the elderly population in the community. However, this concern is somewhat minimized by the observation that we treated patients 80 years of age and older at the same rates as those younger patients once registered at MDACC, although fewer patients 80 years of age and older were treated with platinum doublets. Patients 80 years of age and older with a poor PS who were treated with nonplatinum doublets had statistically superior survival than younger patients treated with nonplatinum doublets. Whether this observation is an accident of the multiple comparisons done, the small numbers of patients in this subgroup or resulting from underestimating the performance status in patients 80 years or older as summarized below is unclear.

To further assess this, we did subset analyses controlling for PS and platinum-doublet administration. Interestingly, there was a more exaggerated difference in these subsets than seen in the populations of older versus younger patients overall. It is possible that patients 80 years of age and older who actually have a PS of 1 are often assumed by virtue

Copyright © 2007 by the International Association for the Study of Lung Cancer

of their age to have a PS of ≥2. Because the prognosis of those who migrated, although worse than that for other members of the PS 0/1 group could be better than those who actually have a PS of 2/3 in the poor PS group, survival rates would increase in each group. This would only be true if the patients 80 years of age and older who had a PS of 1 who were misassigned actually had on average a worse PS of 1 than the patients with a PS of 1 who were correctly assigned to the PS 0/1 group. Indeed, this possibility is also supported by the fact that a larger percentage of patients 80 years of age and older were assigned a PS of ≥2. Alternatively, in older patients, there may be a greater likelihood of noncancer causes of a poor PS that do not confer as poor a prognosis as cancer-induced poor PS. Whether either or both of these are true requires further study. However, it does draw attention to the concern that we are perceiving elderly patients as being less able to tolerate therapy than they actually are.

There may be other types of bias as well. Thus as a retrospective study, information on toxicity and dosing is not as detailed and reliable as would be the case for patients treated in a clinical trial. This limits our ability to draw firm conclusions regarding regimen tolerability because there may be under- or overreporting of toxicity. In addition, because our information on dosing was derived from the clinic notes that reliably indicated the type of chemotherapy and schedule but typically did not include the doses, it is possible that some of the doses may have been lower in some of the patients older than 80 years of age. On that basis, it therefore may have been more tolerable in the older population. In addition, some data indicate that older patients tend to have more indolent tumors, which, if so, would confound the ability to determine the survival benefit from chemotherapy.[24] However, the similar response rates observed in the older and younger groups of our study suggest that many of the older patients did apparently benefit from the chemotherapy.

In summary, our data showed that selected patients 80 years of age and older may tolerate and apparently benefit from commonly used chemotherapy regimens, including platinum doublets. A patient's physiologic age rather than chronologic age may be the critical determinant of which type of chemotherapy to choose. However, determining a patient's physiologic age is challenging because we often assume the physiologic age is older than it is due to age bias. Although our analysis was retrospective, our results are consistent with those of other retrospective studies of elderly patients younger than 70 years old. We believe that our results are compelling enough to merit a prospective study of patients 80 years of age and older. This will help us determine whether this large and growing subset of NSCLC patients might benefit from our most effective regimens. In addition, to speed up the assessment of whether patients 80 years of age and older benefit from standard chemotherapy as well as novel agents, increased efforts to include representative numbers of these patients in clinical trials needs to be considered.

REFERENCES

1. Parkin DM. Global cancer statistics in the year 2000. *Lancet Oncol* 2001;2:533–543.
2. Ihde DC. Chemotherapy of lung cancer. *N Engl J Med* 1992;327:1434–1441.
3. Chemotherapy in non-small cell lung cancer—a metaanalysis using updated data on individual patients from 52 randomized clinical trials. Non-small Cell Lung Cancer Cooperative Group. *BMJ* 1995;311:899–909.
4. Goodwin PJ, Shepherd FA. Economic issues in lung cancer: review. *J Clin Oncol* 1998;16:3900–3912.
5. Sandler AB, Gray R, Brahmer J, et al. Randomized phase II/III trial of paclitaxel (P) plus carboplatin (C) with or without bevacizumab (NSC # 704865) in patients with advanced non-squamous non-small cell lung cancer (NSCLC): an Eastern Cooperative Oncology Group (ECOG) Trial E4599. In Abstracts of the 2005 ASCO annual meeting, May 13–17, 2005, Orlando, FL, abstract no. LBA4.
6. Fossella F, DeVore R, Kerr R, et al. Randomized phase III trial of docetaxel versus vinorelbine or ifosfamide in patients with advanced non-small cell lung cancer previously treated with platinum-containing chemotherapy regimens. *J Clin Oncol* 2000;18:2354–2362.
7. Hanna N, Shepherd FA, Fossella FV, et al. Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell lung cancer previously treated with chemotherapy. *J Clin Oncol* 2004;22:1589–1597.
8. Shepherd FA, Rodrigues Pereira J, Ciuleanu T, et al. Erlotinib in previously treated non-small-cell lung cancer. *N Engl J Med* 2005;353:123–132.
9. Surveillence Epidemiology and End Results (SEER) Website. Available at http://www.seer.cancer.gov/statfacts/html/lungb_print.html. Accessed October 20, 2005.
10. Gridelli C, Aapro M, Ardizzoni A, et al. Treatment of advanced non-small-cell lung cancer in the elderly: results of an international expert panel. *J Clin Oncol* 2005;1:23:3125–3137.
11. Lilenbaum RC, Herndon JE II, List MA, et al. Single-agent versus combination chemotherapy in advanced non-small-cell lung cancer: the cancer and leukemia group B (study 9730). *J Clin Oncol* 2005;23:190–196.
12. Chen YM, Perng RP, Chen MC, et al. A phase II trial of vinorelbine plus gemcitabine in previously untreated inoperable (stage IIIb/IV) non-small-cell lung cancer patients aged 80 or older. *Lung Cancer* 2003;40:221–226.
13. Period Life Table, 2001; available at http://www.ssa.gov/OACT/STATS/table4c6.html. Accessed October 23, 2005.
14. Fitzpatrick AL, Kuller LH, Ives DG, et al. Incidence and prevalence of dementia in the Cardiovascular Health Study. *J Am Geriatr Soc* 2004; 52:195–204.
15. Skoog I, Nilsson L, Palmertz B, Andreasson LA, Svanborg A. A population-based study of dementia in 85-year-olds. *N Engl J Med* 1993;328:153–158.
16. Ramsey SD, Howlader N, Etzioni RD, Donato B. Chemotherapy use, outcomes, and costs for older persons with advanced non-small-cell lung cancer: evidence from surveillance, epidemiology and end results-Medicare. *J Clin Oncol* 2004;22:4971–4978.
17. Hutchins LF, Unger JM, Crowley JJ, et al. Underrepresentation of patients 65 years of age or older in cancer-treatment trials. *N Engl J Med* 1999;341:2061–2067.
18. Hesketh PJ, Lilenbaum R, Chansky K, et al. Chemotherapy in patients >80 with advanced non small cell lung cancer: combined results from SWOG 0027 and LUN 6. In Abstracts of the 2005 ASCO annual meeting, May 13–17, 2005, Orlando, FL, abstract no. 7147.
19. Hotta K, Ueoka H, Kiura K, Tabata M, Tanimoto M. An overview of 48 elderly-specific clinical trials of systemic chemotherapy for advanced non-small cell lung cancer. *Lung Cancer* 2004;46:61–76.
20. Repetto L, Balducci L. A case for geriatric oncology. *Lancet Oncol* 2002;3:289–297.
21. Repetto L, Venturino A, Fratino L, et al. Geriatric oncology: a clinical approach to the older patient with cancer. *Eur J Cancer* 2003;39:870–880.
22. Gridelli C, Perrone F, Gallo C, et al. Chemotherapy for elderly patients with advanced non-small-cell lung cancer: the Multicenter Italian Lung Cancer in the Elderly Study (MILES) phase III randomized trial. *J Natl Cancer Inst* 2003;95:362–372.
23. Di Maio M, Perrone F, Gallo C, et al. Supportive care in patients with advanced non-small-cell lung cancer. *Br J Cancer* 2003;89:1013–1021.
24. Borges M, Sculier JP, Paesmans M, et al. Prognostic factors for response to chemotherapy containing platinum derivatives in patients with unresectable non-small cell lung cancer. *Lung Cancer* 1996;16:21–33.

Copyright © 2007 by the International Association for the Study of Lung Cancer